

(19)



Europäisches Patentamt
European Patent Office
Office européen des brevets



(11)

EP 1 264 547 A1

(12)

EUROPEAN PATENT APPLICATION

(43) Date of publication:
11.12.2002 Bulletin 2002/50

(51) Int Cl.7: **A23L 1/226, C11B 9/00,**
C07C 321/20, C07C 327/22

(21) Application number: 01113787.4

(22) Date of filing: 06.06.2001

(84) Designated Contracting States:
AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU
MC NL PT SE TR
Designated Extension States:
AL LT LV MK RO SI

- Ratcliff, Damian John
Singapore 267935 (SG)
- Furrer, Stefan
Cincinnati 45208, Ohio (US)

(71) Applicant: **Givaudan SA**
1214 Vernier-Genève (CH)

(74) Representative: **Simmons, John Murray, Dr.**
Givaudan Duebendorf AG,
Überlandstrasse 138
8600 Dübendorf (CH)

(72) Inventors:
• **Grab, Willi**
Singapore 278733 (SG)

(54) **Flavour and fragrance compositions**

(57) **Flavour and fragrance compositions comprising 1-mercapto-1-arylalkanes or derivatives thereof.**

EP 1 264 547 A1

Description

[0001] This invention is concerned with flavour and fragrance compositions containing 1-mercapto-1-arylalkanes, in particular 1-mercapto-1-phenylalkanes and to methods of flavouring or adding fragrance or aroma to a food, beverage or a consumer healthcare or household product using these compounds.

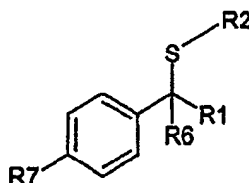
[0002] The flavour and fragrance industry is continuously interested in new ingredients that may impart to a product a clear, natural spicy, roasted and fruity character.

[0003] Both benzylmercaptan and 2-phenylethylmercaptan have found use in the flavours industry for the strong roasted note that they impart to meat and coffee flavours. However, the use of these compounds in the flavours industry is limited, and of practically no use in the fragrance industry, because of their characteristic dominant roasted note which is also accompanied by pungent and slightly putrid notes.

[0004] It might be expected that molecules possessing a similar structure to benzylmercaptan and 2-phenylethylmercaptan would express similar characteristic notes. In fact, just such a structurally similar molecule - 1-mercapto-1-phenylethane - has been found in volatiles of the defence secretion of skunks and in the volatiles of fermented household waste.

[0005] Surprisingly, however, we have now found that certain 1-mercapto-1-arylalkanes and derivatives thereof impart to products the clear, natural spicy, roasted and fruity character so desired by the flavour and fragrance industry, without any attendant dominant roasted note or accompanying pungent and putrid notes.

[0006] Accordingly, the invention provides in one of its aspects a flavour or fragrance composition comprising a compound of formula (I)



wherein R1 represents an alkyl group having from 1 to 4 carbon atoms which may be branched or unbranched; R2 represents, hydrogen; acyl, in particular selected from the group $-(R3)C=O$ wherein R3 represents a branched or unbranched alkyl group having from 1 to 4 carbon atoms; or an alkoxyalkyl group, in particular selected from the group $-CH(R4)-OR5$, wherein R4 represents hydrogen or a branched or unbranched alkyl group having from 1 to 4 carbon atoms; R5 represents a branched or unbranched alkyl group having from 1 to 4 carbon atoms; R6 represents hydrogen or methyl; and R7 represents hydrogen, methyl or alkoxy having 1 to 4 carbon atoms, e.g. methoxy.

[0007] R1, R3, R4 and R5 independently are particularly represented by methyl, ethyl, n-, or iso-propyl, and n-, or iso-butyl. R2 is particularly represented by hydrogen, formyl, acetyl, propionyl, butyryl, isobutyryl, 1'-ethoxyethyl, 1-methoxyethyl, or 2'-(2'-methoxypropyl).

[0008] Particularly preferred compounds for use in compositions according to the invention are selected from 1-mercapto-1-phenylethane, 1-mercapto-1-phenylpropane, 1-mercapto-1-phenylbutane, 1-mercapto-1-phenylisobutane, 1-mercapto-1-(p-methylphenyl)-ethane, 1-mercapto-1-(p-methylphenyl)-propane, and 2-mercapto-2-(p-methylphenyl)-propane. Most preferred are 1-mercapto-1-phenylethane, 1-mercapto-1-phenylpropane and 2-mercapto-2-(p-methylphenyl)-propane.

[0009] A compound of formula (I) may be used in its enantiomerically pure form, however, as the R and S enantiomers were found to have essentially similar activity as flavour or fragrance materials, it is preferred to use the more easily accessible and therefore cheaper racemate.

[0010] The mercapto-compounds of formula (I) (i.e. $R2 = H$) are known and may be synthesised from commonly available starting materials and reagents according to synthetic protocols known in the art. Acylmercapto-compounds (i.e. $R2 = \text{acyl}$), e.g. acetylmercapto-compounds of the formula (I) may be synthesised from the corresponding alcohol, e.g. 1-phenyl-1-propanol, and thioacetic acid in the presence of zinc chloride according to standard synthetic protocols known in the art. Alkoxyalkylmercapto compounds of formula (I) (i.e. $R2 = \text{alkoxyalkyl}$) may be formed, for example by reacting the corresponding mercapto-compound with, for example ethyl-vinyl-ether under acid catalysis according to standard synthetic protocols.

[0011] The resolution of the compounds of the formula (I) into their enantiomeric forms may also be effected in a manner known in the art.

[0012] Compositions according to the present invention may contain one or more compounds of the formula (I).

Alternatively, the compositions may contain one or more precursors of compounds of the formula (I). By "precursors" is meant certain derivatives that may be transformed into a compound of formula (I), for example over an extended period of time during storage, and/or as a result of the application of an exogenous physical stimulus, for example the application of heat and/or light to the product containing said precursors, or by some chemical stimulus such as hydrolysis, e.g. enzymatic hydrolysis. As a further alternative, a composition according to the invention may contain one or more compounds of formula (I) and one or more precursors. Precursors independently may have properties as flavourants or odourants.

[0013] As precursors come into consideration, in particular, thioesters of compounds of formula (I), in particular thioesters of lower fatty acids, e.g. C₁ to C₆ fatty acids, and carbonates of compounds of the formula (I). These precursors may be obtained by reacting a compound of formula (I) with an acyl chloride. Other precursors include thioacetals of lower aldehydes, for example acetaldehyde and propionaldehyde, which may be obtained by reacting the corresponding mercapto-compound with, for example an alkyl-vinyl-ether.

[0014] It is to be understood that certain compounds of formula (I), whereas they are useful as flavourants and odourants in their own right, may act as precursors for certain other compounds of formula (I), for example, those compounds wherein R = acyl or alkoxyalkyl may act as precursors for compounds wherein R = H.

[0015] The flavourant and odourant qualities of compounds of the formula (I) and precursors thereof may be evident over a broad range of concentrations. For example, in the case of a food, a beverage, a consumer healthcare product or a household product a compound or precursor may be present in amounts ranging from 0.0001 to 500mg/Kg, more preferably 0.01 to 50mg/Kg. Whereas, in the case of a fragrance composition a compound or a precursor may be present in a concentration ranging from 0.001% to 10%, more preferably 0.01% to 1.0%.

[0016] The compounds of formula (I) and/or precursor compounds may be mixed with any ingredients useful in flavour or fragrance compositions. In particular, they may be combined with one or more of the extensive range of natural, synthetic, nature identical, natural odourant or flavourant materials or natural extracts used in the flavour or fragrance fields.

[0017] Additionally, compositions may contain one or more ingredients or excipients commonly used in conjunction with flavourants and odourants, for example carrier materials, thickeners, flavour enhancers and other auxiliary agents commonly known and used in the art.

[0018] Compositions according to the invention may be employed in all the customary fields of application. Particular embodiments of the invention include compositions for use in fragrance applications, for example fine fragrance applications or perfumed products of all kinds, for example luxury perfumes, cosmetic articles, consumer healthcare products or household products, e.g. washing agents, detergents, soaps and toothpaste. Other particular embodiments include the use in flavour applications, for example in foodstuffs, beverages, pharmaceuticals, oral hygiene products and other healthcare products wherein it is customary to use flavourants.

[0019] The compounds of formula (I) and/or their precursor compounds add fruity, spicy and some tropical aspects to fruit flavour and vegetable compositions such as citrus, chilli and papaya. The top note of the flavour of such products is increased and modified in a natural direction. However, the use of compounds of formula (I) is not limited to fruit flavours. Thus, compounds of the present invention may be combined with savoury, herbal and mint flavours to enhance natural herbal and spicy flavours. In a particular embodiment, compounds of formula (I) may be used to enhance the natural spicy aroma and flavour of Asian curry flavours.

[0020] There now follows a series of examples that serve to illustrate the invention.

Synthesis Examples

Thioacetic acid S-(1-phenyl-ethyl) ester:

[0021] In a synthesis carried out according to Gauthier, Bourdon, Young, Tetrahedron Lett., 27(1), 15 (1986), at room temperature, 16.3g of zinc iodide, 100mL of dichloromethane and 12.5g of 1-Phenyl-1-ethylalcohol are added to a 250mL round-bottom flask. To this suspension 9.52g of thioacetic acid is added. The mixture is stirred for 16 hours at room temperature. The reaction mixture is extracted with dichloromethane. The organic layer is washed with brine, dried over magnesium sulphate, filtered and concentrated to give 18.2g of yellow liquid which is purified by chromatography on silica gel.

1-Mercapto-1-phenylethane:

[0022] In a synthesis carried out according to Hoppe, et al., Angew. Chem. Int. Ed., 36(24), 2784 (1997), at room temperature, 2.1g of lithium aluminum hydride and 100mL of methyl tertiary butyl ether are added to a 250mL round-bottom flask. To this suspension 18g of thioacetic acid S-(1-phenyl-ethyl) ester in 50mL MTBE is added. The mixture is stirred for 15h at room temperature. 5mL of ethyl acetate and 2.5mL of sodium hydroxide (1M in water) are added.

The reaction mixture is filtered over a sodium sulphate plug. The filtrate is concentrated to give 13.7g of yellow liquid which is purified by distillation.

(S)-1-Mercapto-1-phenylethane:

[0023] In a synthesis carried out according to EP-0480716, Merck Frosst Canada Inc., (1992), and Hoppe, et al., Angew. Chem. Int. Ed., 36(24), 2784 (1997), at -10°C, 2.6g of triphenyl phosphine and 35mL tetrahydrofuran are added to a 100mL round-bottom flask. To this solution 1.74g of diethyl azo dicarboxylate are added. The solution is stirred for 8 hours at -10°C, at which time it became a beige suspension. A solution of 0.61g of (R)-1-Phenyl-1-ethanol, 0.78g of thioacetic acid in 7.5mL tetrahydrofuran is added at -10°C. The mixture is stirred for 16 hours at room temperature. The reaction mixture is concentrated, suspended in hexane and filtered. The filtrate is washed with brine, dried over magnesium sulfate, filtered, concentrated and purified by column chromatography on silica gel to give 0.58g yellow liquid. This is reacted as described in the synthesis of 1-mercapto-1-phenylethane as described above to give 0.35g of (S)-1-mercapto-1-phenylethane.

Thiobutyric acid S-(1-phenyl-ethyl) ester:

[0024] At room temperature, 13.8g of 1-mercapto-1-phenylethane is dissolved in 50mL of butyryl chloride. The mixture is stirred at room temperature for 6 hours. It is then cooled down to 0 °C and the reaction is quenched by careful addition of 100ml of dry methanol in small portions. The mixture is then washed with bicarbonate, dried over magnesium sulfate, filtered and concentrated to give the butyrate compound in 98% yield.

1-(Methylthio)-1-phenylethane:

[0025] At 0 °C, 2.24g sodium thiomethoxide and 25mL tetrahydrofuran are added to a 100mL flask. 5.89g (1-bromoethyl)benzene in 5mL tetrahydrofuran are added and the mixture is stirred for 16 hours at room temperature. The reaction mixture is extracted with MTBE/brine. The organic layer is washed with brine, dried over magnesium sulfate and concentrated to give the methylthio compound in 90% yield.

[0026] Table 1 discloses compounds of the general formula set forth below, that may be formed according to an appropriate method analogous to those described above, employing corresponding starting materials. In all cases, the compounds are formulated into fragrance compositions to provide sparkling and diffusive accords, and into foods and beverages to impart strong fruity or spicy aspects.

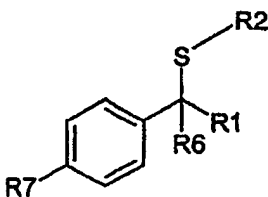


Table 1

Ex	R1	R2 ^(a)	R6	R7
1	methyl	H	H	H
2	ethyl	H	H	H
3	n-butyl	H	H	H
4	methyl	H	H	methyl
5	methyl	H	H	methoxy
6	methyl	H	methyl	H
7	methyl	methyl	H	H
8	methyl	A	H	H
9	ethyl	A	H	H
10	n-butyl	A	H	H
11	methyl	A	H	methyl
12	methyl	A	H	methoxy
13	methyl	B	H	H

Table 1 cont.

14	methyl	C	H	H
15	methyl	D	H	H
16	methyl	A	methyl	H
17	methyl	E	H	H



(a) = The residues A through E are represented by the formula:-

wherein in residue A, Y = methyl ; in residue B, Y = ethyl ; in residue C, Y = propyl ; in residue D, Y = iso-propyl ; and in residue E, Y = hydrogen.

Formulation Example 1

[0027] 0.08mg/l, 1-mercapto-1-phenyl-ethane was added to a tropical fruit soft drink of composition (a) containing the fruit flavour (b). Comparing the resultant composition with the aroma note of the starting soft drink, an additional typical top note was detected and, at the same time, the persistence was increased significantly.

(a): Composition of typical tropical fruit soft drink:

[0028]

	[g]
water	9400
orange juice concentrate	100
sugar syrup 65 Brix	170
citric acid 50%	5

(continued)

	[g]
sodium citrate	0.4
sodium benzoate	0.15
tropical fruit flavour (b)	10

(b): Composition of tropical fruit flavour

[0029]

Lemon oil green	100
Tangerine oil cold pressed	300
Orange oil 7.8 fold	200
Sinensal fraction ex orange oil	5
Ethyl butyrate	10
Allylhexanoate	5
Acetaldehyde	30
Orange oil Brazil	340
Key component (1% in Triacetin)	10

Formulation Example 2

[0030] The effect of 1-mercapto-1-phenyl-ethane, and the structurally similar molecules benzylmercaptan and 2-phenylethylmercaptan on an orange soft drink (blank) was examined.

[0031] The aforementioned compounds were added at a level of 0.1 mg/L and compared with the blank orange soft drink. The drink containing 1-mercapto-1-phenyl-ethane exhibited an orange, mandarin, fresh squeezed juice note with strong fruity aspects, typical of oranges found in Asia, which is a significant improvement over the blank soft drink. In contrast thereto, the drinks containing benzylmercaptan or 2-phenylethylmercaptan had a strong roasted, even slightly putrid note, which did not blend well with the fruity aspect.

Composition of orange soft drink:

[0032]

	[g]
water	9500
sugar syrup 65 Brix	170
citric acid 50%	5
sodium citrate	0.4
sodium benzoate	0.15
orange oil 40 fold	0.005

Formulation Example 3

[0033]

<u>Curry sauce</u>	
Sugar	120.0
Xanthan Gum	0.40
Salt	60.0
Citric Acid	0.80
Modified Starch Coflo 67	24.0

(continued)

Curry sauce	
Ground Onion Powder	48.0
Ground Garlic Powder	10.0
Ground Curry Powder	20.0
Soyarome	5.6
Tomato Paste	33.6
Vegetable Oil	104.0
Water	560.0
Chicken Flavour	2.4
Gourmax Coconut Milk	8.0
Curry Flavour	3.2
Total	1000.0

Preparation Method (Laboratory Scale)

[0034]

- 1) Xanthan gum and sugar were premixed and left to one side.
- 2) The remaining ingredients, except flavours, were added to a pot and cooked at medium heat until the sauce started to thicken. The premix of gum and sugar were added and cooking continued until the temperature reached 85 degrees centigrade. Thereafter, the sauce was left to stand for at least 5 minutes. Afterwards, the flavours were added and stirred well to dissolve. The sauce was then filled into glass bottles and sterilised. Optionally a preservative such as sodium benzoate is added to prolong the shelf life.

Curry Flavour	
Anise Oil	0.6
Clove Oleoresin	0.3
Coriander Oleoresin	24.0
Cumin Oleoresin	8.0
Cinnamon Oleoresin	0.6
Ginger Oleoresin	2.0
Black Pepper Oleoresin	3.0
Oleoresin Turmeric	8.0
Palm Olein	q.s.
Capsicum Oleoresin	30.0
Total	1000.0

[0035] The addition of 0.01% of a 1% solution of 1-mercapto-1-phenyl-ethane added a very natural spicy note to the curry sauce, which was well appreciated by Indian and Asian people. The addition of 0.01% of a 1% of benzylmercaptan or 2-phenylethylmercaptan conversely, added a burnt, roasted note to the curry sauce.

Formulation Example 4

Comparison of fragrance accords:

[0036] Either 0.004 % (w/w) of 1-mercapto-1-phenyl-ethane, benzylmercaptan or 2-phenylethylmercaptan were added to a clementine accord as described below. At a very low level the accord turned from orange to a natural mandarin with 1-mercapto-1-phenyl-ethane. The sample was more sparkling, natural clementine and strongly diffusive. When benzylmercaptan or 2-phenylethylmercaptan were used instead, the samples were less diffusive and a disturbing sulphurous, burnt, putrid side note appeared.

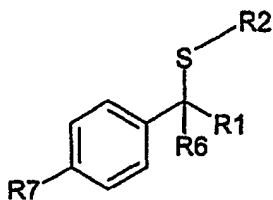
Formula of clementine accord

[0037]

5	rose oxide	1
	buchu leaf oil	2
	geranyl acetate	3
	geranyl butyrate	3
10	ethyl caprylate	4
	(E)-2-hexenal	4
	geranyl isobutyrate	4
	cinnamic aldehyde	5
15	oxane 5% in dipropylene glycol	5
	hexanal	6
	(Z)-3-hexenol	6
	linalool oxyd	6
	isoeugenol acetate	7
20	corps pampelmousse 10% in triethyl citrate	10
	benzaldehyde	15
	allyl heptanoate	15
25	cinnamyl acetate	20
	beta ionone	24
	ethyl acetoacetate	60
	gamma undecalactone	80
	ethyl acetate	120
30	labienoxime	200
	lemon oil Italy	600
	furonol 1% in triethyl citrate	1060
	orange oil 7-fold	2000
	orange oil brasil	2400
35	dipropylene glycol	3340
		10000

Claims

1. A flavour or fragrance composition comprising a compound of the formula (I)



wherein R1 represents an alkyl group having from 1 to 4 carbon atoms which may be branched or unbranched; R2 represents, hydrogen; acyl, in particular selected from the group $-(R3)C=O$ wherein R3 represents a branched or unbranched alkyl group having from 1 to 4 carbon atoms; or an alkoxyalkyl group, in particular selected from the group $-CH(R4)-OR5$, wherein R4 represents hydrogen or a branched or unbranched alkyl group having from 1 to 4 carbon atoms; R5 represents a branched or unbranched alkyl group having from 1 to 4 carbon atoms; R6 represents hydrogen or methyl; and R7 represents hydrogen, methyl or alkoxy having 1 to 4 carbon atoms.

2. A composition according to claim 1 wherein R1 is represented by methyl, ethyl, n-, or iso-propyl, and n-, or iso-butyl.
3. A composition according to claim 1 or claim 2 wherein R2 is represented by hydrogen, acetyl or 1'-ethoxyethyl.
- 5 4. A composition according to any of the preceding claims wherein the compound of formula (I) is selected from 1-mercapto-1-phenylethane, 1-mercapto-1-phenylpropane, 1-mercapto-1-phenylbutane, 1-mercapto-1-phenylisobutane, 1-mercapto-1-(p-methylphenyl)-ethane, 1-mercapto-1-(p-methylphenyl)-propane, and 2-mercapto-2-(p-methylphenyl)-propane.
- 10 5. A flavour or fragrance composition comprising 1-mercapto-1-phenylethane in the form of its thioester, thioacetal, thioacetate, thioformate or thioacetaldehyde-ethylacetal.
6. A flavoured product comprising a compound of formula (I) as defined in claim 1 present in an amount ranging from 0.0001 to 500mg/kg, more preferably 0.01 to 50mg/kg.
- 15 7. A flavoured product according to claim 6 selected from a food, a beverage, pharmaceutical, oral hygiene product or healthcare product.
- 20 8. A fragranced product comprising compound of formula (I) defined in claim 1 present in an amount ranging from 0.001% to 10%, preferably 0.01% to 1%.
9. A fragranced product according to claim 8 wherein the fragranced product is a fine fragrance or perfumed product selected from a cosmetic, or a consumer healthcare or household product selected from a washing agent, a detergent, a soap or a toothpaste.
- 25 10. A composition according to any of the preceding claims comprising a precursor of a compound of formula (I) in addition to, or in place of, a compound of formula (I).
- 30 11. A method of improving a flavour or fragrance composition comprising the step of adding thereto a compound of formula (I) or a precursor thereof.

35

40

45

50

55



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 01 11 3787

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Y	ARCTANDER: " PERFUME AND FLAVOR CHEMICALS (AROMA CHEMICALS)" 1969 , MONCLAIR, S. ARCTANDER , US XP002182406 189660 * example 325 *	1-11	A23L1/226 C11B9/00 C07C321/20 C07C327/22
Y,D	J. Y. GAUTHIER: "A mild and efficient synthesis of thiolesters from alcohols" TETRAHEDRON LETTERS. , vol. 27, no. 1, 1986, pages 15-18, XP002182405 ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM.; NL * the whole document *	1-11	
A	US 3 968 264 A (STOLL MAX ET AL) 6 July 1976 (1976-07-06) * the whole document *	1-11	
			TECHNICAL FIELDS SEARCHED (Int.Cl.7)
			A23L C11B C07C
The present search report has been drawn up for all claims			
Place of search THE HAGUE		Date of completion of the search 9 November 2001	Examiner Dauksch, H
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application I : document cited for other reasons S : member of the same patent family corresponding document</p>			

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 01 11 3787

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

09-11-2001

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 3968264 - A	06-07-1976	US 4138410 A	06-02-1979
		US 3989713 A	02-11-1976
		US 3976802 A	24-08-1976
		US 3985906 A	12-10-1976
		US 3922366 A	25-11-1975
		US 3943260 A	09-03-1976
		US 3949100 A	06-04-1976
		US 3947603 A	30-03-1976
		US 3978241 A	31-08-1976
		US 3950566 A	13-04-1976
		US 4018910 A	19-04-1977
		US 4000328 A	28-12-1976
		US 3940502 A	24-02-1976
		US 3917872 A	04-11-1975
		US 3900581 A	19-08-1975
		US 4005227 A	25-01-1977
		US 3917871 A	04-11-1975
		US 3961095 A	01-06-1976
		US 3900582 A	19-08-1975
		US 4038435 A	26-07-1977
		US 3924015 A	02-12-1975
		US 3931245 A	06-01-1976
		US 3931246 A	06-01-1976
		US 3931166 A	06-01-1976
		US 3993792 A	23-11-1976
<hr/>			